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FILE 'HOME' ENTERED AT 12:38:17 ON 23 AUG 2002

=> fil reg

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

0.21

0.21

FULL ESTIMATED COST

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Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> Uploading 10049904.str

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 12:38:52 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS SEARCH TIME: 00.00.01

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 33 TO 447 PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s 11 full

Examiner Anderson 703-605-1157

10049904 Page 3 08/23/2002

FULL SEARCH INITIATED 12:38:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 173 TO ITERATE

100.0% PROCESSED 173 ITERATIONS

SEARCH TIME: 00.00.01

13 ANSWERS

L3 13 SEA SSS FUL L1

=> d scan

10049904 Page 4 08/23/2002

L3 13 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-{(2,4-dioxo-5-thiazolidinyl)methyl}-2-methoxy-N-{(4'-methoxy(1,1'-biphenyl]-4-yl)methyl}- (9CI)
MF C26 H24 N2 O5 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 13 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-{(2,4-dioxo-5-thiazolidiny1)methy1}-2-methoxy-N-{(4'-methy1|1,1'-bipheny1)-4-y1)methy1}- (9C1)
MF C26 H24 N2 O4 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

L3 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(3-methoxyphenoxy)phenyl]methyl]- (9CI)
MF C26 H24 N2 O6 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

10049904 Page 5 08/23/2002

=> fil caplus COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 140.28 140.49

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=> s 13 L4 1 L3

=> d ibib abs hitstr

Examiner Anderson 703-605-1157

10049904 Page 6 08/23/2002

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:152660 CAPLUS DOCUMENT NUMBER: 134:193427 TITLE: PRACTICE PRACT

134:193427
Preparation of substituted benzylthiazolidine-2,4dione derivatives as agonists of human peroxisome
proliferator-activated receptor
Miyachi, Hiroyukir Nomura, Masahiro; Tanase, Takahiro;
Murakami, Koji; Tsunoda, Masaki
Kyorin Pharmaceutical Co., Ltd., Japan
PCT Int. Appl., 20 pp.
CODEN: PIXXO2
Patent

INVENTOR(S):

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001014351 A1 20010301 WO 2000-JP5521 20000818

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GB, GB, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, KX, NO, NZ, PL, PT, RO, RU, SD, ES, GS, SI, SS, SI, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, WW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CT, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1207157 A1 2020522 EP 2000-93477 20000818

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO::

JP 1999-235529 A 19990823

GTHER SOURCE(S):

MARPAT 134:193427

G1 KIND DATE APPLICATION NO. DATE

The title compds, represented by general formula (I; wherein A represents optionally substituted Ph, optionally substituted phenoxy or optionally substituted benzyloxy), pharmaceutically acceptable salts thereof and hydrates of the same are prepd. These compds, are capable of, as a ligand of human peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level. Thus, 5-[(2,4-dioxxthiazolidin-5-ylmethyl]-2-methoxybenzoic acid, EIN, and CH2C12 were mixed, treated with Et chlorocarbonate under ice-cooling, and stirred for

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS (Continued) 326925-79-5 CAPLUS Benzamide, 5-[(2.4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-phenoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

326925-80-8 CAPLUS
Benzamide, 5-[{2,4-dioxo-5-thiazolidinyl)methyl}-2-methoxy-N-[{4-{2-methoxyphenoxylphenyl}methyl}- (9CI) (CA INDEX NAME)

326925-81-9 CAPLUS Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(3-methoxyphenoxy)phenoxy)methyl]- (9CI) (CA INDEX NAME)

326925-82-0 CAPLUS Benzamide, 5-[{2,4-dioxo-5-thiazolidinyl}methyl]-2-methoxy-N-[{4-{4-

Examiner Anderson 703-605-1157

Answer 1 of 1 CAPLUS COPYRIGHT 2002 ACS (Continued)

10 min under ice-cooling, followed by adding a solm. of
4-benzyloxybenzylamine in CH2C12, and the resulting mixt. was stirred at
room temp, for 2 h to give 771 N- [(4-benzyloxyphenz)] methyl]-5-[(2,4dioxothiazolidin-5-yl]methyl]-2-methoxybenzamide (II). II and I (A = Pho)
enhanced the transcriptional activity of human PPAR.alpha. in CHO cells
with EC50 of 0.44 and 0.24 .mu.M, resp.
26925-73-73 26925-87-84-9 26925-79-5p
26925-80-19 326925-81-99 326925-83-9
326925-83-1P 326925-84-2P 326925-83-3P
326925-83-1P 326925-84-2P 326925-88-6P
326925-89-79
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted benzylthiazolidinedione derivs. as agonists of
human peroxisome proliferator-activated receptor and blood sugar and
lipid-lowering agents)

lipid-lowering agents)
326925-77-3 CAPUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(phenylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326925-78-4 CAPLUS
Benzamide, N-([1,1'-biphenyl]-4-ylmethyl)-5-((2,4-dioxo-5-thiazolidinyl)methyl}-2-methoxy- (9CI) (CA INDEX NAME)

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS (Continued) methoxyphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326925-83-1 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(3-methylphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326925-85-3 CAPLUS
Benzamide, N-[(4'-chloro[1,1'-biphenyl]-4-yl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

10049904 Page 7 08/23/2002

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 326925-86-4 CAPLUS
CN Benzanide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methoxy[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)

RN 326925-87-5 CAPIUS
CN Benzamide, N-[[4-[(4-chlorophenyl)methoxy]phenyl]methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

RN 326925-88-6 CAPLUS CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-[(4-

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS (Continued) methylphenyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

RN 326925-89-7 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methyl]1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10049904 Page 8 08/23/2002

| => fil reg | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 4.79 | 145.28 |
| | | |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -0.62 | -0.62 |

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=> Uploading 10049904.str

L5STRUCTURE UPLOADED

=> dL5 HAS NO ANSWERS L5 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 15 full FULL SEARCH INITIATED 12:41:00 FILE 'REGISTRY' 10049904 Page 9 08/23/2002

FULL SCREEN SEARCH COMPLETED -211 TO ITERATE

100.0% PROCESSED 211 ITERATIONS 56 ANSWERS

SEARCH TIME: 00.00.01

56 SEA SSS FUL L5 L6

=> fil caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION 140.66 285.94 FULL ESTIMATED COST DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -0.62

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=> s 15

REG1stRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress... Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 12:41:07 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED -13 TO ITERATE

100.0% PROCESSED 13 ITERATIONS

2 ANSWERS

10049904 Page 10 08/23/2002

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 44 TO 476
PROJECTED ANSWERS: 2 TO 124

L7 2 SEA SSS SAM L5

L8 2 L7

=> fil caplus

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
0.40 287.12

FULL ESTIMATED COST 0.40 287.12

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE 0.00 -0.62

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=> s 15

REG1stRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress... Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

10049904 Page 11 08/23/2002

SAMPLE SEARCH INITIATED 12:41:26 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 13 TO ITERATE

100.0% PROCESSED 13 ITERATIONS 2 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE** BATCH **COMPLETE**

PROJECTED ITERATIONS:

44 TO 476

PROJECTED ANSWERS:

2 TO 124

L9 2 SEA SSS SAM L5

L10 2 L9

=>

=>

=>

=>

=>

=> =>

=> fil caplus

SINCE FILE COST IN U.S. DOLLARS TOTAL SESSION FULL ESTIMATED COST 0.40 288.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -0.62

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=> s 16 L11 33 L6

=> fil reg
COST IN U.S. DOLLARS

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
0.40 288.70

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -0.62

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=> d scan 16

10049904 Page 13 08/23/2002

56 ANSWERS REGISTRY COPYRIGHT 2002 ACS Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-(phenylmethyl)- (9CI) C19 H18 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L6 56 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-trifluoromethyl)phenyl]methyl]-, monopotassium salt (9C1)
MF C20 H17 F3 N2 O4 S . K

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

56 ANSWERS REGISTRY COPYRIGHT 2002 ACS Benzamide, N-[(3,4-dichlorophenyl)methyl]-5-[(2,4-dioxo-5-thiaoclidinyl)methyl]-2-methoxy- (9CI) C19 H16 C12 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L6 56 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(1-methyl)ethoxy)phenyl]methyl]- (9CI)
MF C22 H24 N2 O5 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

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L6 56 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(4-chlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI)
MF C19 H17 C1 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L6 56 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methyl[1,1'-biphenyl]-4-yl)methyl]- (9CI)
MF C26 H24 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

10049904 Page 15 08/23/2002

=> s 16 not 13 L12 43 L6 NOT L3

=> d scan 112

Examiner Anderson 703-605-1157

10049904 Page 16 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-(1,3-benzodioxol-5-ylmethyl)-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI)
MF C20 H18 N2 O6 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):42

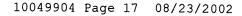
L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N(phenylmethyl)- (9CI)
MF C19 H18 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidiny1)methy1]-2-methoxy-N-[(4-nitropheny1)methy1]- (9C1)
MF C19 H17 N3 O6 5

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT **

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methoxyphenyl)methyl]- (9CI)
MF C20 H20 N2 O5 5



L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl)-2-methyl-N-[[4-trifluoromethyl)phenyl]methyl]- (9CI)
MF C20 H17 F3 N2 03 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Glycine, N=[(4-bromo-2-fluorophenyl)methyl]-N-[3-[(2,4-dioxo-5-thiazolidinyl)methyl]benzoyl]- (9CI)
MF C20 H16 Br F N2 OS S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluctomethoxy)phenyl]methyl]- (9CI)
MF C20 H17 F3 N2 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-hydroxy-N-[{4-(trifluoromethyl)phenyl}methyl]- (9CI)
MF C19 H15 F3 N2 04 5

10049904 Page 18 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-{(2,4-dioxo-5-thiazolidinyl)methyl}-2-methoxy-N-[[4-(trifluoromethyl)phenyl)methyl]-, monopotassium salt, monohydrate (9CI)
MF C20 H17 F3 N2 O4 S . H2 O . K

● K

● н20

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[{2,4-dioxo-5-thiazolidinyl}methyl]-2-methoxy-N-[{4-methylphenyl}methyl]- (9CI)
MF C20 H20 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidiny1)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl]methyl]- (9CI)

F C20 H17 F3 N2 O4 S
CI COM

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4(trifluoromethyl)phenyl]methyl]-, monopotassium salt (9CI)
MF C20 H17 F3 N2 O4 S . K

Examiner Anderson 703-605-1157

10049904 Page 19 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(3,5-bia)ctrifluoromethyl)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl)-2-methoxy- (9C1)
MF C21 H16 F6 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[[4(trifluoromethyl)phenyl]methyl]- (9CI)
MF C19 H15 F3 N2 03 5.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, monosodium salt, monohydrate (9CI)
MF C20 H17 F3 N2 O4 S . H2 O . Na

Na

● H₂O

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-fluoro-N-[[4-trifluoromethyl]phenyl]methyl]- (9CI)
MF C19 H14 F4 N2 O3 S

10049904 Page 20 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS

Benzamide, 5-{(2,4-dioxo-5-thiazolidinyl)methyl}-2-methoxy-N-methyl-N(phenylmethyl)- (9CI)

MF C20 H20 N2 O4 S

CH2

CH2

C-N-CH2-Ph

OMe O Me

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, monosodium salt (9CI)
MF C20 H17 F3 N2 O4 S. Na

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[(2,4-dioxo-5-thiazolidiny1)methy1]-2-methoxy-N-[[4-(trifluoromethy1)pheny1]methy1]- (9CI)
MF C20 H17 F3 N2 O4 S
C1 COM

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-ethyl-2-methoxy-N-[[4(trifluoromethyl)phenyl]methyl]- (9CI)
MF C22 H21 F3 N2 04 5

10049904 Page 21 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(3,4-dichlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI)
MF C19 H16 C12 N2 04 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, compd. with (R)-.alpha.-methylbenzenemethanamine (1:1) (9CI)
MF C20 H17 F3 N2 O4 S . C8 H11 N

CM 1

CM 2

Absolute stereochemistry.

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-4-methoxy-N-(phenylmethyl)- (9CI)
MF C19 H18 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(2,4-dichlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI)
MF C19 H16 C12 NZ O4 S

10049904 Page 22 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-(1,3-benzodioxol-5-ylmethyl)-3-[(2,4-dioxo-5-thiazolidinyl)methyl)-4-methoxy- (9CI)
MF C20 H18 N2 O6 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-propoxyphenyl)methyl]- (9C1)

MF C22 H24 N2 OS 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Benzamide, 3-(12,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl)methyl]-, compd. with (S)-.alpha.methylbenzenemethanamine (1:1) (9CI)

MF C20 H17 F3 N2 O4 S . C8 H11 N

CM 1

Absolute stereochemistry

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-4-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI)
MF C20 H17 F3 N2 O4 S

10049904 Page 23 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-hydroxy-N-[[4(trifluoromethyl)phenyl]methyl]- (9CI)
MF C19 H15 F3 N2 04 5.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidiny1)methy1]-N-[(4-fluorophenyl)methy1]-2-methoxy- (9CI)
MF C19 H17 F N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(1-methylethoxy)phenyl]methyl]- (9CI)
MF C222 H24 N2 O5 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-(1-methylethoxy)-N-[[4(trifluoromethyl)phenyl]methyl]- (9CI)
MF C22 H21 F3 N2 O4 S

10049904 Page 24 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-{(2,4-dioxo-5-thiazolidiny1)methy1}-N-{(4-ethy) benylemy1|methy1}-2-methoxy- (9CI)
MF C21 H22 N2 05 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-(1,3-benzodioxol-5-ylmethyl)-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-ethoxy- (9CI)
MF C21 H20 N2 O6 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(3,4-dimethoxyphenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI)
MF C21 H22 N2 O6 5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[3-(trifluoromethoxy)phenyl]methyl]- (9CI)
MF C20 H17 F3 N2 O5 S

10049904 Page 25 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(4-(1,1-dimethylethyl)phenyl]methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI)
MF C23 H26 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-ethoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI)
MF C21 H19 F3 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(4-chlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9C1)
MF C19 H17 C1 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[2-trifluoromethyl)phenyl]methyl]- (9CI)
MF C20 H17 F3 N2 04 S

10049904 Page 26 08/23/2002

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(4-(dimethylamino)phenyl]methyl)-5-[(2,4-dioxo-5thiazolidinyl)methyl]-2-methoxy- (9CI)
MF C21 H23 N3 04 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[{3-(trifluoromethyl)phenyl]methyl}-(9CI)
MF C20 H17 F3 N2 04 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

L12 43 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzamide, N-[(4-bromophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]2-methoxy- 9c1
MF C19 H17 Br N2 O4 S

10049904 Page 27 08/23/2002

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=> s 111 and PPAR 2658 PPAR 406 PPARS 2700 PPAR

(PPAR OR PPARS)

L13 17 L11 AND PPAR

=> d ibib abs hitstr 1-17

10049904 Page 28 08/23/2002

L13 ANSWER 1 OF 17
ACCESSION NUMBER:
TITLE:
Benzopyrancarboxylic acid derivatives with
PPRA apoints activity for the treatment of
diabetes and lipid disorders, and their preparation,
pharmaceutical compositions, and use
Sahoo, Soumya P.r. Koyama, Hiroor Miller, Daniel J.;
BOURCE:
USA
U.S. PATENT ASSIGNEE(S):
US. PAT. Appl. Publ., 42 pp.
CODEN: USXXCO
Patent

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator

INVENTOR(S):

PATENT TYPE:

LANGUMENT TY

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 2002055299 A1 20020530 US 2001-808457 20010314

PRICARTY APPIM. INFO.: US 2000-266528P P 20000315

AB Methods and compns. are disclosed for the treatment of diabetes, obesity and diabetic-related conditions. The methods include gene therapy based administration of a therapeutically effective ant. of vectors encoding the following: glucokinase regulatory protein alone or co-administered with glucokinase or with metab. modifying proteins or oglucokinase co-administered with glucokinase or with metab. modifying proteins; or squeckinase equilatory protein co-administered with glucokinase in combination with metab. modifying proteins, to a diabetic patient. The metab. modifying proteins, to a diabetic patient. The metab. modifying proteins include UCP2, UCP3, PPAR. alpha., OB-Rb, GUP-1 and GUP-1 analogs (administered via vector or directly as a peptide). Preferred examples of GUP-1 analogs include GUP-1-G1y8, Extendin-4 and the "Black Widow" chimeric GUP-1 analog. Addnl., PPAR. alpha. ligands and DPP-IV inhibitors may be co-administered with the above.

IT 213252-19-8, KPR-297

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study), USES (Uses) (gene therapy for treatment of diabetes and related conditions)

RN 21252-19-8 CAPIUS

CN Benzamide, 5-[(2,4-dioxo-5-chiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

L13 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued) activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDOM), hyperplycemia, dyslipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular testenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or productus are disclosed (wherein: Z = C12, CO) Rl = M, CH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or Rl forms (un)substituted cyclopropane fusion to adjacent C atomix, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; RM = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or RSM or ARMS = (un)substituted 5- or 6-membered heterocyclic ringl. A list of 29 compds. is claimed, and their prepn. is described. For example, Et 7-hydroxy-d-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc with PhCHZO(CHZ)3BF (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz(4,5)isoxazole (45%), and (7) alk, hydrolysis (100%), to give title compds. II PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a no. of specific drugs, is claimed.

17 21325-19-6, KPR-297
RI: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (therapeutic compns. also contg., prepn. of benzopyrancarboxylic acid derivs. as PPAR agonists for treatment of diabetes and lipid dis

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002013864 A1 20020221 WO 2001-JP7037 20010815
W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU,
SG, SK, US, ZA
RV: AT, BE, CH, CY, DE, DX, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR
JZ 2002128700 A2 20020509 JP 2001-241740 20010809
AU 2001078738 A5 20020225 AU 2001-78779
PRIORITY APPLN. INFO.:

JP 200218700 A2 20020509 JP 2001-241740 20010809
AJ 200108738 A5 20020225 AJ 2001-241740 20010809
AJ 2001078738 A5 20020225 AJ 2001-78738 20010815
PRIORITY APPLA INFO.: JP 2000-2002246910 A 20000816
JP 2000-2002246910 A 20000816
JP 2000-2002246910 A 20000816
OTHER SOURCE(S): MARPAT 136:177669
AB Disclosed are medicinal compns, for preventing or treating cancer wherein one or more Peroxisome proliferator-activated receptor .gamma. (
PPAR, gamma.) activation agonists are used simultaneously or successively. A combined administration of 5-[4-(6-methoxy-1-quality) and targetin 100 mg/kg to HL-60 cell-bearing mice showed synergistic antitumor effect. Also, table to were preped. from I 0.004, targretin 0.1, lactose 0.244, corn starch 50, and magnesium stearate 0.002

RISTRU (Therapeutic use); BIOL (Biological study); USES (Uses) (simultaneous or successive use of PPAR, gamma. agonists and RXR agonists for prevention or treatment of cancer) 213252-19-8 CAPUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromathyl)phenyl]methyl]- (SCI) (CA INDEX NAME)

10049904 Page 29 08/23/2002

L13 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 17
ACCESSION NUMBER:
DOCUMENT NUMBER:
1171LE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002013812 A1 20020221 W0 2001-US25668 20010816

W: AU, CA, MX, NZ, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR
AU 2001089271 A5 20020225 AU 2001-88271 20010816

PRIORITY APPLN. INFO:: US 2000-235907 P 20000817

NW: AT. BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
AU 2001088271 A5 20020225 AU 2001-88271 20010816

RRITY APPLN. INFO:
US 2000-2255907 P 20000906
WO 2001-US2568 W 20010816

The present invention describes methods for the use of PPAR
ligands in the treatment inflammatory endocrine, dermatol., cardiovascular
immunol., neurol., ophthalmic, neoplastic, pulmonary diseases, and
age-related dysregulations. In addn., methods are provided for treating
said conditions and diseases comprising the step of administering to a
human or an animal in need thereof a therapeutic mat. of pharmacol.
compns. comprising a pharmaceutically acceptable carrier, and a
PPPAR gamma. agonist which cross-activates PPAR alpha. or
PPPAR.gamma./RVR agonist, effective to reverse, slow, stop,
or a PPAR.gamma./RVR agonist, effective to reverse, slow, stop,
or prevent the pathol. inflammatory or degenerative process.
212322-19-8, KRP 297

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(methods for treating inflammatory diseases using PPAR
agonists)
21252-19-8 CAPLUS
Benzamide, 5-((2,4-dioxo-5-thizolidinyl)methyl)-2-methoxy-N-[[4(trifluoromethyl)phenyl]methyl]- (SCI) (CA INDEX NAME)

L13 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2002 ACS

2

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 17
ACCESSION NUMBER:
DOCUMENT NUMBER:
115:15:1071
TITLE:
INVENTOR(S):
PATENT ASSIGNEE(S):
PATENT ASSIGNEE(S):
POURCE:
POUR ASSIGNEE(S):
POURCE:
DOCUMENT TYPE:
DOCUMENT TYPE:
Patent
LANGUAGE:
PATENT
ASSIGNEE(S):
POURCE:
DOCUMENT TYPE:
Patent
LANGUAGE:
English

LANGUAGE: English 1 LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

NFORMATION:

ENT NO. XIND DATE APPLICATION NO. DATE

2002008188 A1 20020131 W0 2001-US22979 20010720

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MY, MX, MZ, NO, AZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, VX, YU, ZA, ZW, AM, AZ, EY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GM, GQ, GW, ML, MR, NE, SN, TD, TG

2002042441 A1 20020411 US 2000-220778P P 20000725 PATENT NO. WO 2002008188 US 2002042441 PRIORITY APPLN. INFO.: OTHER SOURCE(S): GI

10049904 Page 30 08/23/2002

ANSWER 5 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB The title indoles having aryloxyacetic acid substituents [1, R1 = Me, optionally substituted with 1-3 F atoms; R2-R4 = H, halo, alkyl, etc.; R5, R6 = H, F, OH, alkyl, and R5 and R6 groups that are on the same carbon atom optionally may be joined to form a cyclopropyl group; R7, R8 = H, F, alkyl, or CR7R8 may form cycloakkyl; R9 = H, alkyl; Arl = (un)substituted Ph, naphthyl, pyridyl, quinolyl; X = CO, SO2, CH2, CHMe, CMe2, CF2, cyclopropylidene; Y = O, S n = O-5] which are agonists or partial agonists of PPAR gamma, and are useful in the treatment, control or prevention of non-insulin dependent diabetes mellitus (NIDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertiglycediemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR mediated diseases, disorders and conditions, were prepd. E.g., a multi-step synthesis of (25)-II was given.

Given. 2

213252-19-8, KRP-297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. of N-substituted indoles for treating diabetes)

213252-19-8 CAPLUS

Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[{4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

REFERENCE COUNT:

40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:900080 CAPLUS DOCUMENT NUMBER: 136:318816

TITLE:

AUTHOR(S):

Ids: 138016
Design, synthesis and evaluation of substituted phenylpropanoic acid derivatives as peroxisome proliferator-activated receptor (PPAR) activators: novel human PPAR alpha.-selective activators Miyachi, Miroyuki; Nomura, Masahiro; Tanase, Takahiro; Takahashi, Kulie; Ide, Tomohiro; Tsunoda, Masaki; Murakami, Koji; Awano, Katsuya; Kyorin Pharmaceutical Co., Ltd., Discovery Research Laboratories, Tochigi, Shimotsuga-gun, Nogi-machi, 329-0114, Japan Bioorganic & Medicinal Chemistry Letters (2001), Volume Date 2002, 12(1), 77-80. CODEN: BMCLER; ISSN: 0960-894X Elsewier Science Ltd. Journal CORPORATE SOURCE:

SOURCE:

PUBLI SHER:

DOCUMENT TYPE: LANGUAGE:

JEHER: Elsevier Science Ltd.

MENT TYPE: Journal

UNGE: English
A series of substituted phenylpropanoic acid derivs. was prepd. as part of
a search for subtype-selective human peroxisome proliferator-activated
receptor (PPAR) activators. Structure-activity relationship
studies indicated that the substituent at the .alpha.-position of the
carboxyl group plays a key role in detg. the potency and the selectivity
for PPAR transactivation.
213252-19-8, KRP 297

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(design, synthesis and evaluation of substituted phenylpropanoic acid
derivs. as PPAR activators)

Benzamide, S-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10049904 Page 31 08/23/2002

ACCESSION NUMBER: 2001:617987 CAPLUS COPYRIGHT 2002 ACS COCUMENT NUMBER: 135:1805757
TITLE: Preparation 135:180757
Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and lipid disorders Liu, Kun: Xu, Libo, Jones, A. Brian Merck + Co. Inc., USA PCT Int. Appl., 54 pp. CODEN: PIXXD2 Patent English 1 INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| P | ATE | TKE | NO. | | KI | ND | DATE | | | A | PPLI | CATI | ON N | ٥. | DATE | | | | |
|------|---------------------|------|------|-----|-----|-----|------|------|------|-----|------|------|------|------|------|------|-----|-----|--|
| - | | | | | | | | | | - | | | | | | | | | |
| W | 0 2 | 2001 | 0608 | 07 | A | 1 | 2001 | 0823 | | W | 0 20 | 01-ປ | 5463 | 6 | 2001 | 0214 | | | |
| | | w: | ΑE, | AG, | AL, | AM, | AT, | AU, | AZ, | BA, | BB, | BG, | BR, | BY. | BZ, | CA, | CH. | CN. | |
| | | | | | | | DK, | | | | | | | | | | | | |
| | | | ΗU, | ID, | IL, | IN, | 15, | JP, | KE, | KG, | KR, | KZ, | LC, | LK. | LR. | LS, | LT. | LU. | |
| | | | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NO, | NZ, | PL. | PT. | RO. | RU. | SD. | |
| | | | SE, | SG, | SI, | SK, | SL, | TJ, | TM, | TR, | TT. | TZ. | UA. | UG. | US. | UZ. | VN. | YU. | |
| | | | ZA, | ZW, | AM, | AZ, | BY, | KG, | KZ, | MD, | RU, | TJ. | TM | | | | | , | |
| | | RW: | GH, | | | | | | | | | | | ZW. | AT. | BE. | CH. | CY. | |
| | | | | | | | FR, | | | | | | | | | | | | |
| | | | | | | | CM, | | | | | | | | | | | , | |
| ORI | ORITY APPLN. INFO.: | | | | | | | | | | | | | 2000 | | | | | |
| ER : | sou | RÇE | (S): | | | MAR | PAT | 135: | 1807 | 57 | | | | | | | | | |
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$$R^5$$
 Y
 R^4
 R^4
 R^2
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The title compds. (I) [wherein Rl and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl or Rl and R2 may form a cycloalkyl group: R3 and R4 = independently (fluoro)alkyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = 0, S, nor NR; Z = 0 or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and

L13 ANSWER 9 OF 17
ACCESSION NUMBER:
DOCUMENT NUMBER:
135:175429
Modulation of bone formation with peroxisome proliferator-activated receptor activators and ligands
PATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:
DOCUMENT TYPE:
DAMGHAGP:
PATENT ASSIGNEE(S):
FOR THE PROPRIES OF THE PROPRIES

MANUUAGE: ratent English FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO. XIND DATE APPLICATION NO. DATE

WO 2001060355 A1 20010823 W0 2001-GB626 20010215

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, CM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HJ, ID, IL, IN, IS, JF, KE, KG, KF, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, WH, MC, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TH, TR, TT, TZ, UA, UG, US, UZ, VM, TU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GG, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZV, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO:

AB The use of an activator or ligand of a peroxisome proliferator-activated receptor, other than PPRR gamma. or pharmaceutically acceptable deriv. of said activator or ligand in the manuf. of a medicament for the treatment or prophylaxis of bone disease allows, for the first time, bone anabolism to enhance the deposition of bone in conditions which would benefit from increased bone deposition. The reverse, where there is inhibition and/or retardation of bone deposition is also facilitated.

IT 213252-19-8, RMP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(modulation of bone formation with peroxisome proliferator-activated receptor activators and ligands)

RN 213252-19-8 CAPIUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-{{4-

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT:

Examiner Anderson 703-605-1157

L13 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued) prodrugs thereof] were prepd. For example, 2.4-dihydroxy-3,5-dipropyl-1',1'-trifluoroacetophenone oxine was acctylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzioxazole. Etherification with Me .alpha.-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by sapon., afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) .alpha. and/or .gamma. and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycenia, dyslipidemia, hypercipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR.alpha. and/or .gamma. mediated diseases, disorders, and conditions (no data).

IT 213252-19-8, KRP-297
RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministration with; prepn. of benzisoxazolyloxyacetic acid

(Uses)
(Coadministration with; prepn. of benzisoxazolyloxyacetic acid PPAR agonists via cyclization of dihydroxyacetophenone oximes for treatment of diabetes and lipid disorders)
213252-19-8 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMA

L13 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued) RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10049904 Page 32 08/23/2002

ACCESSION NUMBER:

DOCUMENT NUMBER:

DOCUMENT NUMBER:

DOCUMENT NUMBER:

DOCUMENT NUMBER:

DOCUMENT NUMBER:

AUTHOR(S):

AUTHOR(S):

AUTHOR(S):

AUTHOR(S):

Brooks, Dawn A.; Etgen, Garret J., Rito, Christopher J.; Shuker, Anthony J.; Dominianni, Samuel J.; Warshawsky, Alan M.; Ardecky, Robert; Paterniti, James R.; Tyhonas, John; Karanewsky, Donald S.; Kauffman, Raymond F.; Broderick, Carol L.; Oldham, Brian A.; Montrose-Rafizadeh, Chabradi Winneroski, Leonard L.; Faul, Margaret H.; McCarthy, James R.

CORPORATE SOURCE:

CORPORATE SOURCE:

Lilly Research Laboratories A Division of Eli hilly Company Lilly Corporate Center, Indianapolis, IN, 46285, USA

SOURCE:

SOURCE:

DUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

DISTRIBUTED AND AND ISSN: 0022-2623

American Chemical Society

DOCUMENT TYPE:

LANGUAGE:

English

Propionic acid deriv. I, which was designed and synthesized based on putative pharmacophores of known PPAR.gamma.— and PPAR. alpha.—selective compds., exhibits potent dual PPAR. alpha.—selective compds., exhibits potent dual PPAR. alpha.—gamma. agonist activity as demonstrated by in vitro binding and dose overlap in the newly introduced EOB mouse model for glucose lowering and lipid/cholesterol homeostasis.
213252-19-8, KRP-297
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Uses)
(design and synthesis of 2-methyl-2-[4-[2-(5-methyl-2-sryloxazol-4-yl)sthoxy]phenoxy]propionic acids: a new class of dual PPAR alpha./.gamma.agonists)
213252-19-8 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

L13 ANSWER 11 OF 17
ACCESSION NUMBER:
DOCUMENT NUMBER:
134:34620
Solid oral composition containing KRP-297
Ohyama, Toshinori; Imamizu, Masaru
Kyorin Pharmaceutical Co., Ltd., Japan
COEN: PIXXU2
DOCUMENT TYPE:
LANGUAGE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
1
COPPLIANT 2002 ACS
2001:359797 CAPLUS
201:359797 CAPLUS
201:359

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. APPLICATION NO. DATE

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001034148 Al 20010517 WO 2000-JP7905 20001110

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MN, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPIN. INFO: JP 1999-320586 A 19991111

AB Disclosed are solid compns. for oral use for facilitating the administration in a small dose of KRP-297, which is a ligand common to peroxisome proliferator-activated receptors PPAR, alpha, and PPAR, gamma. (i.e., nuclear receptors) and has an effect of ameliorating insulin resistance, which contain the drug ingredient together with pharmaceutical carriers, it is possible to provide tablets which contain the drug component in a uniform content and can be easily and quant. taken. By preps, solid compns. for oral use composed of a trace amt. of the drug ingredient together with pharmaceutical carriers, it is possible to provide tablets which contain the drug component in a uniform content and can be easily and quant. taken. By preps, solid compns. for oral use composed of a trace amt. of the drug ingredient together with pharmaceutical carriers, it is possible to provide tablets which contain the drug component in a uniform content and can be easily and quant. taken. By preps, solid compns. for oral use composed of a trace amt. of the drug ingredient together with pharmaceutical carriers, it is possible to provide tablets which contain the drug component in a uniform content and can be easily and quant. taken. By preps, solid compns. for oral use to the drug ingredient together with pharmaceutical carriers, it is possible to provide tablets which co

Examiner Anderson 703-605-1157

L13 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2002 ACS

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FO

L13 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

REFERENCE COUNT: THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10049904 Page 33 08/23/2002

L13 ANSWER 12 OF 17
ACCESSION NUMBER:
DOCUMENT NUMBER:
TITLE:

INVENTOR(S):

PATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:

CAPLUS COPYRIGHT 2002 ACS
2001:152661 CAPLUS
134:193428
Preparation of substituted benzylthiazolidine-2,4dione derivatives as agonists of human peroxisome
proliferator-activated receptor
Nomura, Hasabiron Murakami, Kojin Tsunoda, Masaki,
Takahashi, Tukke
Kyorin Pharmaceutical Co., Ltd., Japan
PCT Int. Appl., 19 pp.
COUMENT TYPE:

DOCUMENT TYPE:

ACCESSION NUMBER:
2001:152661 CAPLUS
2011:52661 CAPLUS
2011:526 DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: WO 2001014352 Al 20010301 WO 20000-JF5522 20000918

W: AE, AL, AM, AT, AU, AZ, BA, BB, BC, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DX, DM, EE, ES, FI, GB, GG, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LK, LS, LT, LU, LV, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SX, SL, TJ, TM, TR, TT, UA, UG, VZ, VX, VY, UZ, AZ, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DX, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, NR, NE, SN, TD, TG

EF 1207158 Al 20020522 EP 2000-953478 200000818

R: AT, BE, CH, DE, DX, ES, FR, GB, GR, IT, LI, UU, NL, SE, NC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO:

WO 20010-JP5522 W 20000818

OTHER SOURCE(S):

MARPAT 134:193428 PATENT NO.

The title compds. (I), pharmaceutically acceptable salts thereof and hydrates of the same (wherein RI represents chloro, bromo, nitro, trifluoromethoxy, ethoxy, propoxy or isopropoxy; and RZ represents hydrogen or chloro) are prepd. These compds. are capable of, as a ligand of human peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level; and a process for

L13 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

326926-48-1 CAPLUS
Benzamide, N-[(4-chlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

326926-49-2 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[3-(trifluoromethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326926-50-5 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[(4-ethoxyphenyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued) producing the same. Thus, 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic acid, EtN, and CH2Cl2 were mixed, treated with Et chlorocarbonate and stirred under ico-cooling for 10 min, treated with 4-nitrobenzylamine, and then stirred at room temp. for 2 h to give 75% N-((4-nitrophenyl)methyl]-5-((2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide [11]. II and 1 (R1 = 4-n-Pro, R2 = H] enhanced the transcriptional activity of human PPPR alpha. in CHO cells with EC50 of 0.53 and 0.11 mu.M, resp. 326526-46-3P 326526-50-5P 326526-51-6P 326526-51-9P 326526-52-7P 326526-50-5P 326526-51-6P 326526-52-P 326526-51-5P 5[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide RL: BAC (Riological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of substituted benzylthiazolidinedione derivs. as agonists of human peroxisome proliferator-activated receptor and blood sugar and lipid-lowering agents) 326526-69 CAPLUS Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)

326926-47-0 CAPLUS
Benzamide, N-[(4-bromophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]2-methoxy- (9CI) (CA INDEX NAME)

L13 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

326926-51-6 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(1-methylethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326926-52-7 CAPLUS Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-propoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

326926-53-8 CAPLUS
Benzamide, N-[(2,4-dichlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

Examiner Anderson 703-605-1157

10049904 Page 34 08/23/2002

L13 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS

326926-54-9 CAPLUS
Benzamide, N-[(3,4-dichlorophenyl)methyl]-5-[(2,4-dicxo-5-thiazolidinyl)methyl]-2-methoxy- [9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenoic acid, Et3N, and
CH2Cl2 were mixed, treated with Et chlorocarbonate under ice-cooling, and
stirred for 10 min under ice-cooling, followed by adding a soln. of
4-benzyloxybenzylamine in CH2Cl2, and the resulting mixt was stirred at
room temp. for 2 h to give 77 N F-((4-benzyloxyphenyl)methyl]-5-((2,4dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide [(1]. Il and I (A = PhO)
enhanced the transcriptional activity of human PPAR.alpha. in
CHO cells with ECSO 10.44 and 0.24 a.u.M, resp.
326925-77-39 236925-71-93 236925-78-39-82
326925-83-19 326925-81-99 326925-83-29
326925-83-19 326925-81-99 326925-83-29
326925-83-19 326925-81-99 326925-83-29
326925-80-89 326925-81-99 326925-83-39
326925-80-49 326925-81-99 326925-81-99 326925-81-99
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study); PREF (Preparation); USES (Uses)
[Dio [Biological study); PREF (Preparation); USES (Uses)
(prepn. of substituted benzylthiazolidinedione derivs. as agonists of human peroxisome proliferator-activated receptor and blood sugar and lipid-lowering agents)
RN 326925-77-3 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4(phenylmethoxy)phenyl]methyl]- (SCI) (CA INDEX NAME)

326925-78-4 CAPLUS Benzamide, N-([1,1'-biphenyl]-4-ylmethyl)-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

326925-79-5 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-Examiner Anderson 703-605-1157

L13 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:152660 CAPLUS DOCUMENT NUMBER: 134:193427 Frenaration of the companion of

134:193427
Preparation of substituted benzylthiazolidine-2,4dione derivatives as agonists of human peroxisome
proliferator-activated receptor
Miyachi, Hiroyuki Nomura, Masahiro; Tanase, Takahiro;
Murakami, Koji Tsunoda, Masaki
Kyorin Pharmaceutical Co., Ltd., Japan
PCT Int. Appl., 20 pp.
CODEN: PIXXO2
Patent
Japanese
1

INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.

The title compds. represented by general formula (I; wherein A represents optionally substituted Ph, optionally substituted phenoxy or optionally substituted benzyloxy), pharmaceutically acceptable salts thereof and hydrates of the same are prepd. These compds. are capable of, as a ligand of human peroxisome proliferator-activated receptor (FPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level. Thus,

L13 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS phenoxyphenyl)methyl]- (9CI) (CA INDEX NAME) (Continued)

326925-80-8 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidiny1)methy1]-2-methoxy-N-[[4-(2-methoxyphenoxy)pheny1]methy1]- (9CI) (CA INDEX NAME)

326925-91-9 CAPLUS
Benzamide, 5-(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(3-methoxyphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326925-82-0 CAPLUS
Benzamide, 5-{(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(4-methoxyphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

10049904 Page 35 08/23/2002

L13 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS

326925-83-1 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(3-methylphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326925-84-2 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(4-methylphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

326925-85-3 CAPLUS
Benzamide, N-[(4'-chloro[1,1'-biphenyl]-4-y1)methyl]-5-[(2,4-dioxo-5-

ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued) 326925-88-6 CAPLUS Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-[(4-methylphenyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

326925-89-7 CAPLUS
Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methyl[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT: THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT 27

L13 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continu thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

326925-86-4 CAPLUS
Benzamide, 5-[2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methoxy-1,1'-biphenyl)-4-yl)methyl]- (9CI) (CA INDEX NAME)

326925-87-5 CAPLUS
Benzamide, N-[[4-[(4-chlorophenyl)methoxy]phenyl]methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

L13 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:293502 CAPLUS
DOCUMENT NUMBER: 131:84110

AUTHOR(S): Fenofibrate and Rosiglitazone Lower Serum
CAPURE SOURCE: Triglycerides with Opposing Effects on Body Weight
Chaput, Evelyne, Saladin, Regis; Silvestre, Martine;
Edgar, Alan D.
Department of Metabolic Diseases, Laboratoire
Fournier, Daix, 21121, Fr.
Biochemical and Biophysical Research Communications
(2000), 271(2), 445-450
CODEN: BBRCA9; ISSN: 0006-291X
Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: Academic Press
DOCUMENT TYPE: Journal
AB Activators of peroxisome proliferator activated receptors (PPARS
) are effective drugs to improve the metabolic abnormalities linking
hypertriglyceridemia to diabetes, hyperglycemia, insulin-resistance, and
atherosclerosis. We compared the pharmacol. profile of a PPAR
alpha activator, fenofibrate, and a PPAR, gamma activator,
rosiglitazone, on serum parameters, target gene expression, and body wt.
again in (fa/fa) fatty Zucker rats and db/db mice as well as their assocn.
in db/db mice. Fenofibrate faithfully modified the expression of
PPAR, alpha. responsive genes. Rosiglitazone increased adipose
tissue aPZ mRNA in both models while increasing liver acyl Con oxidase
mRNA in db/db mice but not in fatty Zucker rats. Both drugs lowered serum
triglycerides yet rosiglitazone markedly increased body wt. gain while
fenofibrate decreased body wt. gain in fatty Zucker rats. RFP 297, which
has been reported to be a PPAR, alpha, and agamma. co-activator,
also affected serum triglycerides and insulin in fatty Zucker rats
although no change in body wt. gain in fatty Zucker rats. RFP 297, which
has been reported to be a PPAR, alpha, and agamma. co-activator,
also affected serum triglycerides and insulin in fatty Zucker rats

17 213252-19-8, KRP 297

RL BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); B

REFERENCE COUNT:

THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10049904 Page 36 08/23/2002

L13 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

L13 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

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L13 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:436161 CAPLUS
DICCUMENT NUMBER: 1391:33115
TITLE: Evidence for direct binding of fatty acids and eicosanoids to human peroxisome proliferator-activated receptor .alpha.

AUTHOR(S): Murakami, Koji; Ide, Tomohiro; Suzuki, Masahiro; Mochizuki, Toshiro; Kadowaki, Takashi
CORFORATE SOURCE: Central Research Laboratories, Kyorin Pharmaceutical Co., Ltd., Tochigi, Japan
Biochemical and Biophysical Research Communications (1999), 260(3), 609-613
CODEN: BBRCA9; ISSN: 0006-291X
ACAdemic Press
JOURNAL
LANGUAGE: Academic Press
JOURNAL
LANGUAGE: Academic Press
JOURNAL
AB The .alpha. isoform of peroxisome proliferator-activated receptor (
PPAR) is activated by fatty acids, their metabolites, and the fibrate class of lipid-lowering agents. To test the ability of these activators to directly bind the ligand-binding domain of human
PPAR, alpha, we performed a competitive binding assay using radiolabeled [3H] KRP-297, a known ligand for human PPAR, alpha.
Lingand WT-14,643. Moreover, these natural ligands avidly activated this receptor in a transient transcriptional assay. This study provides the direct evidence that human PPAR.alpha. is activated through the direct evidence that human PPAR.alpha. as a vell as of a fibrate, to its ligand-binding domain. (c) 1999 Academic Press.

IT 21252-19-6, KRP-297
RN: BAC (Biological activity or effector, except adverse); BSU (Biological study); USES (Uses)
(direct binding of fatty acids and eicosanoids to human peroxisome proliferator-activated receptor .alpha.)
RN 21252-19-6 (APPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)
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CH2

CH2

CH2

C-NH-CH2

CF

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Examiner Anderson 703-605-1157

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L13 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

REFERENCE COUNT:

THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:421607 CAPLUS
DOCUMENT NUMBER: 129:239719
TITLE: Effects of PPPAR.alpha. activation on liver
lipid metabolism in Zucker fatty rats
Ide, Tomohico Murakami, Koji; Tobe, Kazuyuki;
Mochizuki, Toshiro Ohashi, Mitsuo: Akanuma, Yasuo;
Kadowaki, Takashi; Yazaki, Yoshio
Corporate Source: Cent. Res. Lab., Kyorin Phara. Co., Ltd., Tochigi,
329-01, Japan
Document Type: Journal
LANGUAGE: Diabetes Frontier (1998), 9(3), 345-346
CODEN: DIFREZ: ISSN: 0915-6593
Medikaru Rebyusha
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Oral administration of KRP-297 or BRL-49653 with high affinity to
PPPAR.alpha. to Zucker fatty (obese) rats and to control lean rats
for 2 wk significantly lowered the blood glucose, insulin, triglyceride,
and free fatty acid levels in the obese rats. KRP-297 and BRL-49653 also
suppressed the increase in triglyceride accumulation and fatty acid
biosynthesis activity in the liver of the obese rats as compared to the
lean rats. In contrast, the markedly reduced activity of the hepatic
acyl-CoA oxidase in the obese rats was markedly recovered by the
administration. The results suggest that the activation of PPAR
.alpha. by KRP-297 or BRL-49653 (ligand) might have inhibitory action on
the hepatic triglyceride accumulation and lipid metab. abnormality in the
obese rats.

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